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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/588,725	08/08/2006	Hashime Kanazawa	2006_1265A	1971

513 7590 12/19/2007

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EXAMINER	
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ART UNIT	PAPER NUMBER
4173	
MAIL DATE	DELIVERY MODE
12/19/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/588,725	KANAZAWA ET AL.	
	Examiner	Art Unit	
	Jonathan S. Lau	4173	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 November 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) *4,5 and 18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3, 6-17 and 19-22* is/are rejected.

7)☒ Claim(s) *2,3,6-9,11-17 and 19-22* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9 pgs/8 Aug 2006, 13 Sep 2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This application is the national stage entry of PCT/JP05/01801, filed 08 Feb 2005; and claims benefit of foreign priority document JAPAN 2004-032329, filed 09 Feb 2004.

Claims 1-22 are pending in the current application. Claim 18, drawn to a non-elected invention, are withdrawn. Claims 4 and 5, drawn to a non-elected species, are withdrawn. Claims 1-3, 6-17 and 19-22 are examined on the merits herein.

Election/Restrictions

Applicant's election of the invention of Group I, claims 1-17 and 19-22, in the reply filed on 26 Nov 2007 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Applicant's species election of fenofibrate as the hyperlipidemic agent and voglibose as the α-glucosidase inhibitor in the reply filed on 26 Nov 2007 is acknowledged.

Specification

The disclosure is objected to because of the following informalities: minor typographical errors, such as:

Page 3, line 11 and page 14, line 10, "dexitrinase", and

Page 18, line 16; page 19, line 4; and page 20, line 25, "gumi".

Appropriate correction is required.

Claim Objections

Claim 2-3, 6-9, 11-17 and 19-22 are objected to because of the following informalities: Dependent claims 2-3, 6-9, 11-17 and 19-22 recite "A pharmaceutical composition according to claim..." It is unclear if the pharmaceutical composition of the dependent claims is the pharmaceutical composition of the independent claims they depend from. This ambiguity is resolved if the dependent claims were to recite "The pharmaceutical composition according to claim..." Examiner has interpreted the dependent claims as being drawn to "The pharmaceutical composition according to claim..."

Appropriate correction is required.

Claim 15 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Claim 1 recites:

"1. A pharmaceutical composition including a combination of (a) at least one hyperlipidemic agent selected from the group consisting of a fibrate compound and a

hydroxymethylglutaryl-CoA reductase inhibitor with (b) an .alpha.-glucosidase inhibitor, wherein the pharmaceutical is

(i) a pharmaceutical composition comprising the hyperlipidemic agent (a) and the .alpha.-glucosidase inhibitor (b), or

(ii) a pharmaceutical combination including a pharmaceutical component comprising the hyperlipidemic agent (a) and a pharmaceutical component comprising the .alpha.-glucosidase inhibitor (b)."

Claim 15 recites:

"15. A pharmaceutical composition according to claim 1, which is

(i) a pharmaceutical preparation comprising (a) a hyperlipidemic agent and (b) an .alpha.-glucosidase inhibitor, or

(ii) a pharmaceutical combination including a pharmaceutical preparation comprising the hyperlipidemic agent (a) and a pharmaceutical preparation comprising the .alpha.-glucosidase inhibitor (b)."

The pharmaceutical preparation of claim 15 does not necessarily comprise the same (a) hyperlipidemic agent and (b) .alpha.-glucosidase inhibitor as the pharmaceutical composition of claim 1 because claim 15 recites "a hyperlipidemic agent" and "an .alpha.-glucosidase inhibitor" rather than "the hyperlipidemic agent" and "the .alpha.-glucosidase inhibitor". Therefore the pharmaceutical composition of claim 15 is not the pharmaceutical composition of claim 1, and claim 15 fails to further limit claim 1.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 12, 14, 20 and 22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 12 and 20 recite "an agent for the prophylaxis or treatment of at least one symptom selected from the group consisting of hyperlipemia, diabetes, diabetes complications, a symptom of hyperglycemia after a meal in diabetics, impaired glucose tolerance (IGT), decrease of glucose tolerance, hypertension, hyperinsulinemia, hyperammonemia, obesity or a complication thereof, fatty liver, and hepatitis." Claims 14 and 22 recite "an agent for the prophylaxis or treatment of at least one symptom selected from the group consisting of diabetes, diabetes complications and a symptom of hyperglycemia after a meal in diabetics."

However, diabetes, hypertension, and hepatitis are diseases, not symptoms. A symptom is a phenomenon that arises from and accompanies a particular disease or disorder and serves as an indication of it. A symptom is not the disease itself. It is unclear what is claimed in claims 12, 14, 20 and 22, whether it is claiming an agent for treatment of a symptom of diabetes, hypertension, or hepatitis; or treatment of the disease of diabetes, hypertension, or hepatitis.

For the purposes of advancing prosecution, Examiner is interpreting the claims as being drawn to an agent for treating a symptom of the disease.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 11-14 and 19-22 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treatment of metabolic syndrome or at least one symptom selected from the group consisting of hyperlipemia, diabetes, diabetes complications, a symptom of hyperglycemia after a meal in diabetics, impaired glucose tolerance (IGT), decrease of glucose tolerance, hypertension, hyperinsulinemia, hyperammonemia, obesity or a complication thereof, fatty liver, and hepatitis (hereafter metabolic syndrome and said symptoms); does not reasonably provide enablement for prophylaxis of metabolic syndrome and said symptoms. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use or make the invention commensurate in scope with these claims.

The Applicant's attention is drawn to *In re Wands*, 8 USPQ2d 1400 (CAFC1988) at 1404 where the court set forth eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:
(1) The nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

Nature of the invention: A pharmaceutical composition which is an agent for the prophylaxis or treatment of metabolic syndrome or at least one symptom selected from the group consisting of hyperlipemia, diabetes, diabetes complications, a symptom of hyperglycemia after a meal in diabetics, impaired glucose tolerance (IGT), decrease of glucose tolerance, hypertension, hyperinsulinemia, hyperammonemia, obesity or a complication thereof, fatty liver, and hepatitis..

The state of the prior art: Prophylaxis is synonymous with prevention. Prevent is defined as "keep from happening or arising; make impossible". See provided definition of prevent (definition of prevent, WordNet, cited in PTO-892). There is no prior art disclosing making metabolic syndrome and said symptoms impossible.

The prior art teaches treatment of metabolic syndrome and said symptoms, for instance improving glycemic control measured as a decrease in plasma glucose, or less pronounced weight gain observed. See Bussolari et al. (US Patent Application Publication US 2003/0045553, published 6 Mar 2003, cited in PTO-892), page 17, paragraph 343. However, the prior art does not teach an absolute absence of increase in plasma glucose or an absolute elimination of any weight gain, indicating these things were not made impossible.

The relative skill of those in the art: The relative skill of those in the art is high.

The predictability or unpredictability of the art: The lack of any prior art disclosing making metabolic syndrome and said symptoms impossible means that one skilled in the art cannot predict the usefulness of a product or method to make metabolic

syndrome and said symptoms impossible. Therefore the claimed invention is unpredictable.

The Breadth of the claims: The scope of the claims specifically includes prophylaxis of metabolic syndrome and said symptoms.

The amount of direction or guidance presented: The specification speaks generally about fibrate compounds inhibiting synthesis or secretion of triglyceride or glucosidase inhibitors inhibiting digestive enzymes. See instant specification, page 1, paragraph 2 and page 3, paragraph 5.

The presence or absence of working examples: The only working examples provided are treatment of metabolic syndrome and said symptoms. For example, see instant specification, page 38, table 1. However, the GLU was not reduced to the level of the untreated control group, indicating treatment did not make metabolic syndrome and said symptoms impossible.

Note that lack of working examples is a critical factor to be considered, especially in a case involving an unpredictable and undeveloped art such as prophylaxis of metabolic syndrome and said symptoms. See MPEP 2164.

The quantity of experimentation necessary: In order to practice the invention with the full range of all possible treatment methods beyond those known in the art, (such as improved glycemic control measured as a decrease in plasma glucose) one skilled in the art would undertake a novel and extensive research program to show that the pharmaceutical composition made metabolic syndrome and said symptoms impossible. Because this research would have to be exhaustive, and because it would

involve such a wide and unpredictable scope of pharmaceutical compositions, treatment methods, and patient populations exhibiting metabolic syndrome and said symptoms, it would constitute an undue and unpredictable experimental burden.

> *Genentech*, 108 F.3d at 1366, sates that, "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion." And "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable."

Therefore, in view of the Wands factors, as discussed above, particularly the breadth of the claims, Applicants fail to provide information sufficient to practice the claimed invention for prophylaxis of metabolic syndrome and said symptoms.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-3, 6-17 and 19-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bussolari et al. (US Patent Application Publication US 2003/0045553, published 6 Mar 2003, cited in PTO-892).

Bussolari et al. discloses a composition for administering one or more glucose readsoprtion inhibitor and one or more PPAR modulator for the treatment of diabetes or Syndrome X, also known as metabolic syndrome (page 1, paragraph 12). Bussolari et al. discloses the specific PPAR modulator fenofibrate (page 8, paragraphs 104 and 129), addressing instant claims 2, 3 and 10. Bussolari et al. discloses the specific α-glucosidase inhibitor voglibose (page 10, paragraph 212 and 219), addressing instant claims 6, 7 and 10. Bussolari et al. discloses a pharmaceutical composition comprising one or more glucose readsorption inhibitor and one or more PPAR modulator (page 12, paragraph 303), addressing instant claims 1 and 15. Bussolari et al. discloses the combination has the advantage of reducing the amount of either drug necessary, thereby reducing one or more adverse side-effects (page 12, paragraph 301), addressing instant claim 17. Bussolari et al. discloses the method of preparing the pharmaceutical composition comprising mixing the active ingredients (page 14, paragraph 323, lines 3-12), addressing instant claim 16. Bussolari et al. discloses the intended use of treating diabetes, Syndrome X, or associated symptoms (page 1, paragraph 12), where Syndrome X and associate symptoms include diabetes, IGT, IFG hyperinsulemia, insulin resistance, dyslipidemia, hypertension, and obesity. (page 1, paragraph 6), addressing the intended use disclosed in instant claims 11-14 and 19-22. Bussolari et al. discloses that "Optimal dosages to be administered may be readily

determined by those skilled in the art, and will vary with the particular compound used, the strength of the preparation, the mode of administration, and the advancement of the disease condition. In addition, factors associated with the particular patient being treated, including patient age, weight, diet and time of administration, will result in the need to adjust dosages." (page 14, paragraph 328). Bussolari et al. discloses the combination of MCC-555, a PPAR modulator, at 3-30 mg/kg and T-1095, a glucose readsorption inhibitor, at 3-100 mg/kg (page 17, paragraph 344, lines 4-6), obviating the ratio of 3 mg/kg glucose readsorption inhibitor to 30 mg/kg PPAR modulator or the ratio of 10 parts be weight voglibose, a glucose readsorption inhibitor, to 100 parts by weight fenofibrate, a PPAR modulator, addressing instant claims 8 and 9.

Bussolari et al. does not specifically disclose the combination of fenofibrate and voglibose.

It would have been obvious to one of ordinary skill in the art at the time of the invention to practice the invention of Bussolari et al. as the specific combination of fenofibrate and voglibose. Bussolari et al. discloses a pharmaceutical composition comprising one or more glucose readsorption inhibitor and one or more PPAR modulator (page 12, paragraph 303). Bussolari et al. discloses the specific α-glucosidase inhibitor voglibose (page 10, paragraph 212 and 219). An α-glucosidase catalyzes the hydrolysis of terminal, non-reducing 1,4-linked α-D-glucose residues with release of α-D-glucose. Inhibition of α-glucosidase would reduce the amount of glucose present to be readsorbed, and therefore inhibit glucose readsorption. Therefore the action of the α-glucosidase inhibitor voglibose results in an inhibition of glucose

readsorption, and voglibose is a glucose readsorption inhibitor. Bussolari et al. discloses the specific PPAR modulator fenofibrate (page 8, paragraphs 104 and 129). It would have been simple substitution of one known element for another to obtain predictable results to use the glucose readsorption inhibitor voglibose and the PPAR modulator fenofibrate. Therefore a pharmaceutical composition of the specific combination of the PPAR modulator fenofibrate and the glucose readsorption inhibitor voglibose, would have been obvious to one of ordinary skill in the art at the time of the invention.

Conclusion

No claims are found to be allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jonathan S. Lau whose telephone number is (571) 270-3531. The examiner can normally be reached on Monday - Thursday, 9 am - 4 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on (571) 272-0718 or Cecilia Tsang can be reached on (571) 272-0562. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

JSL

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614